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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,638	02/08/2007	Mirko Pogutier	2084.7	4364
29494 7590 06/10/2009 HAMMER & ASSOCIATES, P.C. 3125 SPRINGBANK LANE SUITE G CHARLOTTE, NC 28226				
EXAMINER YOUNG, SHAWQUITA				
ART UNIT		PAPER NUMBER		
1626				
MAIL DATE		DELIVERY MODE		
06/10/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/580,638

Applicant(s)

POGUTTER ET AL.

Examiner

SHAWQUIA YOUNG

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 March 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3 and 6-12 is/are pending in the application.
- 4a) Of the above claim(s) 14,15,19 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3 and 6-12 is/are rejected.
- 7) ☒ Claim(s) 2,4,5,13,16 and 18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-20 are currently pending in the instant application. Applicants have amended claims 4, 13, 16 and 18 and cancelled claim 17 in an amendment filed on March 26, 2009. The Examiner wants to point out that Applicants have cancelled claim 17 but left the text in. Usually this error would result in the amendments being non-compliant but the Examiner is sending out this Non-final Office Action in order to expedite prosecution. However, in Applicants' response to this Office Action, the text in claim 17 needs to be deleted.

Claims 1, 3 and 6-12 are rejected, claims 2, 4, 5, 13, 16, and 18 are objected and claims 14,15, 19 and 20 are withdrawn from consideration.

I. *Response to Arguments/Remarks*

Applicants' amendment, filed on March 26, 2009, has overcome the rejection of claims of 13 and 16-18 under 35 USC 112, second paragraph as being indefinite as lacking antecedent basis; the rejection of claims 16-18 under 35 USC 112, second paragraph as being indefinite for failing to clearly describe the crystalline forms A and B; the rejection claim 4 under 35 USC 112, second paragraph for the use of relative language. The above rejections have been withdrawn.

II. *Rejection(s)*

35 USC § 103 - OBVIOUSNESS REJECTION

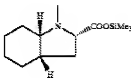
The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). See *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

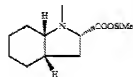
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3 and 6-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Tien, et al.* (US Patent 6,541,635). Applicants claim a method for preparing optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S,3aR,7aS-octahydroindole-2-carboxylic acid} and pharmaceutically acceptable salts thereof, characterized in that a racemic mixture of optionally substituted trans-octahydroindole-2-carboxylic acid is reacted with the N-carboxyanhydride of {N-[1-(S)-alkoxycarbonyl-3-phenylpropyl]-L-alanine}, which is optionally substituted on the phenyl ring, in a suitable inert solvent, and subsequently the resulting optionally substituted {N-[1-S-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindole-2-carboxylic acid} is isolated.



represents various groups including

in an aprotic solvent to form



a protected compound of the formula I wherein R_1 includes

and

the deprotection of the silyl group to obtain the final product (See column 4, lines 35-51).

The Difference Between the Prior Art and the Claims (MPEP §2141.02)

The difference between the prior art of *Tien, et al.* and the instant invention is that there is homologous subject matter. The differences between the prior art and the instant claims are 1) the octahydroindole-2-carboxylic acid is protected with a silyl protecting group; 2) the octahydroindole-2-carboxylic acid is the syn stereoisomer and 3) the reaction includes a deprotection step of the silyl group to obtain the final product.

Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)

Applicants are claiming a process which is a method for preparing optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S,3aR,7aS-octahydroindole-2-carboxylic acid} and pharmaceutically acceptable salts thereof, characterized in that a racemic mixture of optionally substituted trans-octahydroindole-2-carboxylic acid is reacted with the N-carboxyanhydride of {N-[1-(S)-alkoxycarbonyl-3-phenylpropyl]-L-alanine}, which is optionally substituted on the phenyl ring, in a suitable inert solvent, and subsequently the resulting optionally substituted {N-[1-S-carbalkoxy-3-

phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindole-2-carboxylic acid} is isolated.

Applicants' process is open-ended because of the term "characterized" which is considered open-ended language which means that the instant process could include a deprotecting step. Further, the use of deprotecting groups is well known in the art as groups that protect a functional moiety from reacting during a chemical reaction. However, it would be obvious to try to perform a well-known reaction that involves protecting groups without the use of the protecting group in order to shorten the reaction time.

Applicants use a racemic mixture of trans-octahydroindole-2-carboxylic acid in the claimed process wherein the prior art uses the single isomer of syn-octahydroindole-2-carboxylic acid with a protecting group. According to *In re Anthony*, 414 F.2d 1383, 162 USQP 594 (CCPA 1969), a pure optical isomer is not patentable over the racemic mixture unless it possesses properties not possessed by the racemic mixture. Therefore, using a racemic mixture of a starting material wherein the prior art uses a pure isomeric form is not considered unobvious absent unexpected results. Therefore, Applicants have only merely modified a well known reaction wherein the modification is mere optimization by mere modification of routine experimentation and within one skilled in the art.

It would have been obvious for one of ordinary skill in the art to modify a well known reaction by using a racemic mixture of a starting material when the prior art uses a single isomer which is protected. A strong prima facie obviousness has been established.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the limitation “the crystallization is carried out at a temperature” which is dependent on claim 1 but crystallization is not mentioned in claim 1. There is insufficient antecedent basis for this limitation in the claim.

III. *Objections*

Dependent Claim Objections

Dependent Claims 2, 4, 5, 11-13, 16, and 18 are objected to as being dependent upon a rejected based claim. To overcome this objection, Applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim.

IV. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 6:30 AM-3:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626